Structure

In This Issue

CellPress

PH Domain Gets a Double Dose of Grease

PAGE 1977

Jian et al. identify two cooperative lipid binding sites in the PH domain of ASAP1 that regulate the enzymatic activity of ASAP1. The authors speculate that cooperative lipid binding may be a feature of PH domains that control the activity of signaling proteins.

Two-Component Mechanism of srGAP

PAGE 1989

srGAP proteins regulate cell migration and morphogenesis by shaping the structure and dynamics of the cytoskeleton and membranes. Guez-Haddad et al. reveal two structural determinants that allow srGAPs to be recruited and placed accurately at their signaling sites.

Shot of 1918 Flu News

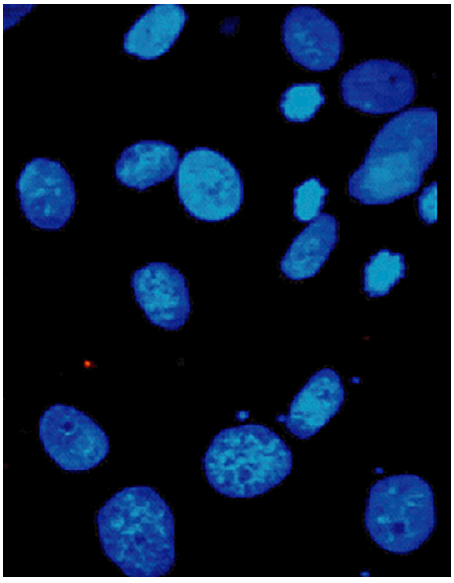
PAGE 2001

Jureka et al. show a direct interaction between the influenza NS1 protein and RIG-I-dependent on the strain of influenza from which NS1 is derived. This occurs at a novel functional region of NS1 that may play a role in modulating strain-dependent influenza virulence.

Negative Design in Protein Structure Prediction

PAGE 2011

Protein stability prediction is a significant challenge. Davey et al. develop a negative computational protein design approach that utilizes native and non-native backbone ensembles to predict mutant sequence stability. This approach enabled the prediction of experimental stability for training and test set Gβ1 sequences.



Sticking a Hairpin in a Type III Secretion System

PAGE 2022

Nguyen et al. present structure of the chaperone-major translocator complex in bacterial type III secretion system, showing that transmembrane regions of the translocator form two hairpins. Both the N- and C-terminal coiled-coil regions remain extracellular after membrane insertion.

Fueling the Biofuels

PAGE 2032

The enzyme 4-coumarate:CoA ligase plays a fundamental role in the biosynthesis of plant secondary metabolite and is a central nexus to several branch pathways. Li and Nair present results of structural, biochemical, and enzyme engineering studies that will allow the use of this enzyme as a tool for biotechnology.

WD-Repeat 48 Interacts with Ubiquitin-Specific Protease 46

PAGE 2043

WD-repeat proteins have been identified as co-factors for USP family deubiquitinases. In a series of novel structures, Yin et al. describe an unprecedented interaction between WDR48 and USP46:ubiquitin. Binding and functional assays validate the interface and extend the insights to USP1, indicative of a prototypical example.

New Class of TPR-like Proteins

PAGE 2055

Tetratricopeptide repeats (TPRs) are ubiquitous protein interaction domains. Marold et al. report the crystal structure of a 42-residue TPR-like array with high (>91%) internal sequence identity and show constructs created from this motif to fold more cooperatively than canonical TPRs.

Switching Small Heat Shock Proteins

PAGE 2066

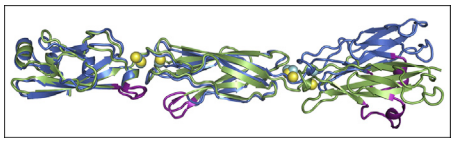
Liu et al. determined the crystal structures of wild-type and mutant SsHsp14.1 with fully visible N-terminal domains. The structural and functional data suggest a new model in which a molecular switch located in N-terminal domain facilitates conformational changes for client protein binding.

Targeting TEAD

PAGE 2076

Pobbati et al. identify a central pocket in the TEAD family of transcription factors that is targetable by small-molecule drugs such as flufenamic acid (FA). FA inhibits TEAD activity and the function of oncogene YAP, which relies on TEAD for its transcriptional activity.

Antiparallel Interactions in Protocadherin



PAGE 2087

Nicoludis et al. determin the structures of two clustered protocadherin fragments and find they form antiparallel complexes. The authors provide a scaffold for isoform-specific interfaces and propose a full-length antiparallel complex that is responsible for homophilic *trans* interactions that mediate self-avoidance during synaptogenesis.

How to Insert Matrix Metalloproteinase-7 into a Membrane

PAGE 2099

Prior et al. examine membrane-binding orientations and allostery in a protease, MMP-7, from linings of organs and tumor cells. Cholesterol sulfate partially inserts and reorients MMP-7 in bilayers. The autoinhibitory conformation is released by remote binding of bicelles, implicating a possible path of allosteric transmission.

Pseudokinase: I'd Rather Be Binding Than Signaling

PAGE 2111

Murphy et al. describe a novel pseudokinase architecture from human TRIB1 and characterize its substrate recognition motif within the C/EBPα transcription factor. Combined with biophysical studies, this shows how Tribbles proteins eschew catalytic activity in favor of function as signaling scaffolds.

A Structural View of Ciliary Function

PAGE 2122

Lokaj et al. biochemically and structurally characterize BARTL1 as an Arl3 effector and speculate on its function in cilia.

Clearing Up All that Collagen

PAGE 2133

Endo180 is an endocytic receptor that clears collagen from the extracellular space. Paracuellos et al. have determined crystal and solution structures of the collagen-binding head of Endo180 and show that the presumed collagen release in endosomes is not regulated by changes within the head.

How Lectin Protects a Pathogenic Fungus

PAGE 2143

Koharudin et al. determine crystal structures of the CVNH-LysM module of MGG_03307, a lectin isolated from *Magnaporte oryzae* that causes serious rice blast disease. Structures in the presence of GlcNAc oligomers, components of the fungal cell wall, illuminate the function of MGG_03307 as a fungal protection protein.

Why mRNA Miscoding Happens

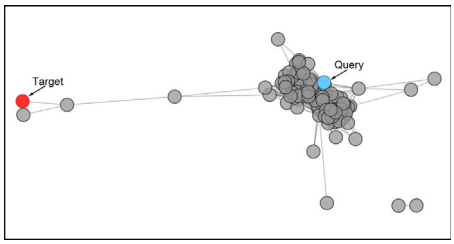
PAGE 2155

Genetic information encoded in mRNA is converted into proteins on the ribosome. Faithful decoding depends on complimentary base pairing between mRNA and tRNA. In this work, Svidritskiy and Korostelev elucidate structural basis for stabilization of a non-complimentary C-C pair, providing insight into mechanisms of mRNA miscoding.

In This Issue

Let's ConTemplate

PAGE 2162



To conduct their function, proteins typically alternate between various conformations, but often only some of these important conformations are known. Narunsky et al. introduce the ConTemplate methodology and webserver for inferring missing conformations of a query protein based on the structural repertoire in the PDB.

Ins and Outs of Dopamine Transport

PAGE 2171

Using advanced molecular modeling, Cheng and Bahar present comprehensive account of dopamine translocation through human dopamine transporter at the atomic level. The study provides a first structural model for a substrate/ion-bound occluded (*holo-occluded*) state transiently stabilized during the transport process.